PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/050334	27.01.2005	28.01.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/4439, A61P1/04, C07D401/12

Applicant
ALTANA PHARMA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Stroeter, T

Telephone No. +49 89 2399-8088

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 8-11

because:

☒ the said international application, or the said claims Nos. 8-11 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-11 (in part)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-11
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11
Industrial applicability (IA)	Yes:	Claims	1-7
	No:	Claims	

2. Citations and explanations

   see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

   and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

   see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 8-11 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item IV

Lack of unity of invention

The application as filed ias considered to lack unity of invention since its subject-matter relates not to one but rather to 5 separate inventions as follows:

Group 1: Claims 1-11 in part insofar as they relate to calcium salts of pantoprazole and (S)-pantoprazoles and hydrates thereof and subject-matter related to these compounds.

Group 2: Claims 1-11 in part insofar as they relate to potassium salts of pantoprazole and (S)-pantoprazoles and hydrates thereof and subject-matter related to these compounds.

Group 3: Claims 1-11 in part insofar as they relate to zinc salts of pantoprazole and (S)-pantoprazoles and hydrates thereof and subject-matter related to these compounds.

Group 4: Claims 1-11 in part insofar as they relate to lithium salts of pantoprazole and (S)-pantoprazoles and hydrates thereof and subject-matter related to these compounds.

Group 5: Claims 1-11 in part insofar as they relate to aluminium salts of pantoprazole and (S)-pantoprazoles and hydrates thereof and subject-matter related to these compounds.

These groups presented in the order chosen by the Applicant are not so linked as to form a single general inventive concept as required by Rules 13.1 and 13.2 PCT for the following reasons:

The common (structural) link between these groups of pantoprazole salts is the (S)-pantoprazole or pantoprazole component which is known (see e.g. the Mg salt disclosed in D5 or the Na salt mentioned in D1 which have the same pharmacological activity) and thus cannot constitute a special technical feature because it does not define a contribution over the prior art. Or, in other words, the structures of the compounds of these five groups have nothing more in common than each of the groups has in common with the mentioned prior art compounds.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Subject-matter of the present application

The present application discloses calcium, potassium, zinc, lithium and aluminium salts of pantoprazole and (S)-pantoprazole which are proton pump inhibitors and are thus useful in the treatment of gastrointestinal disorders.

2 Prior art documents

Reference is made to the following documents. The given numbering will be adhered to in the rest of the procedure:

D1: WO 94/24867 A (SEPRACOR INC) 10 November 1994
D2: WO 99/27917 A (BYK GULDEN LOMBERG CHEM FAB ; NEY HARTMUT (DE); DIETRICH RANGO (DE)) 10 June 1999
D3: WO 02/45686 A (BYK GULDEN LOMBERG CHEM FAB ; LINDER RUDOLF (DE); DIETRICH RANGO (DE)) 13 June 2002
D4: WO 2004/013126 A (HUMMEL ROLF-PETER ; HANAUER GUIDO (DE); KOHL BERNHARD (DE); MUELLER BE) 12 February 2004
D5: WO 00/10995 A (BYK GULDEN LOMBERG CHEM FAB ; KOHL BERNHARD (DE)) 2 March 2000

Concerning document D4 please see item VI.

3 Novelty (Article 33(2) PCT)

The presently claimed Ca-salts are a novel selection of the content of D2 (claim 5) or D3 (page 5, paragraph 3) since such compounds are not specifically disclosed as example compounds. Claims 1-11 insofar as they relate to the first invention (group 1) are novel.

4 Inventive step (Article 33(3) PCT)

It is - at present - not apparent why the presently claimed Ca-salts should be considered to form part of an inventive solution to the problem of providing alternative pantoprazol salts useful as proton pump inhibitors (PPI): Na or Mg salts of racemic or optically active pantoprazole are disclosed in D1-D3 and D5 but it is also anticipated and suggested in the relevant prior art that metals such as Ca can be used as well in order to form other pharmacologically active salts.
The present description states on page 2, last paragraph, that the present salts have unexpected and advantageous properties and refers to stability characteristics and pharmacodynamic/pharmacokinetic properties. However, this statement is not substantiated by experimental data and thus it was not yet shown that the present compounds solve the abovementioned or any other technical problem. Claims 1-11 insofar as they relate to the first invention (group 1) are therefore not inventive.

5 Industrial applicability (Article 33(4) PCT)

The subject-matter of the present claims 1-7 insofar as they relate to the first invention (group 1) is in accordance with the requirements of Article 33(4) PCT.

For the assessment of the present claims 8-11 on the question whether they are

industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI
Certain documents cited

The International Search Report mentions the P-document D4 which does not form part of the state of the art according to Rule 64.1(b) PCT. For the purposes of this communication the priorities of the present application and the above prior art have not been checked and it has been assumed that they are valid. The Applicant is informed, that D4 mentions Ca-salts of pantoprazol rendering the Ca salts of claims 1-11 not novel.

Re Item VII
Certain defects in the international application

The Applicant is informed that, when entering the regional phase at the EPO, an application may contain more than one independent claim in a particular category only certain circumstances. In the present case it appears that present claims 2-4 should be made dependent (on claim 1), as well as claim 7 (on 6) and 9-11 (on 8).